

REMARKS

Claims 1 – 8 are pending in this application. Claims 4 – 8 stand rejected under 35 U.S.C. §112, first paragraph, and Claims 1-4 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Grell, et al. U.S. 4,735,959.

Applicants respectfully traverse the rejections and request reconsideration based on the following remarks, the cancellation of Claim 5, and amendments to Claims 4 and 6.

REJECTION UNDER 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 4 and 5 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirements. Specifically, the Examiner suggested that Claim 4 requires the mechanism as part of its scope and also rejected Claim 5 as a "reach through" claim.

Applicants have cancelled Claim 5 and amended Claim 4 by deleting the language pertaining to the mechanism.

The Examiner rejected Claims 5 – 8 under 35 U.S.C. §112, first paragraph, because the specification is not enabled for disorders responsive to the opening of KCNQ potassium channels in this highly unpredictable art. More specifically, the Examiner states that one of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds of the instant claims.

Applicants have canceled Claim 5 and amended Claim 6 to clearly define the diseases which pertain to the disorders related to the activity associated with KCNQ potassium channel activity. The specification provides both in vitro and in vivo data to support the utility of the claimed compounds. It should be noted that the control compound used in the neuropathic pain model, described on pages 14 and 15, is gabapentin (Neurotin), a drug approved by the FDA for the treatment of convulsions, epilepsy and management of neuralgia (see Physician's Desk Reference).

In addition to the above diseases related to the disorders modulated by KCNQ channels, Applicants believe that the claimed compounds would be useful for the diseases specifically identified in currently amended Claim 6. To support this assertion, the Examiner is directed to Applicants' U.S. Patent 6,831,080 B2 to Wu, *et al.*, issued December 14, 2004. The present Applicants are co-inventors of U.S. 6,831,080 which discloses and claims another but different series of compounds useful in the treatment of the same disorders as claimed in the instant application that are responsive to the opening of the KCNQ potassium channels. In columns 10 to 20 of said U.S. Patent, the Applicants described additional biological tests to confirm the utility of such compounds (KCNQ modulators) for the treatment of mania, bipolar disorders and anxiety. Thus, Applicants believe the instant compounds would have the same utility based on the data presented in the specification.

Furthermore, the Examiner is directed to another application of Wu, *et al.*, which has the same priority date as the instant application and was issued by the USPTO on May 31, 2005, as U.S. Patent 6,900,210. The patent claims a different series of compounds and claims a similar use for the disorders modulated by KCNQ channels.

In view of the cancellation of Claim 5, amendment of Claim 6, and the above remarks, reconsideration of the rejection is respectfully solicited.

REJECTION UNDER 35 U.S.C. §103(a)

Claims 1 – 4 are rejected under 35 U.S.C. §103(a) as being unpatentable over Grell, *et al.*, U.S. 4,735,959. Specifically, the Examiner states that the cited reference teaches carboxylic acid amide compounds and highlights the generic language found in Columns 1 and 2. Further examination reveals a more detailed listing of potential substituents in Columns 3, 4, 5 and 6. More specifically, the Examiner admits that not all R¹ groups are claimed but then states that Grell, *et al.* teach pyridinyl-phenyl and compares this group to Applicants' R¹ substituents.

Applicants respectfully traverse the rejection and disagree with the Examiner's statement that Grell, *et al.* constitutes a *prima facie* obviousness determination that one of ordinary skill in the art would be motivated to prepare the species in Claims 1 – 4 of the instant application.

Applicants reviewed the reference cited by the Examiner and find that Grell, *et al.* discloses compounds which are useful for lowering "blood-sugar" and provides no suggestion or guidance that these compounds may have any other use. In contrast, the compounds of the instant application are modulators of the KCNQ potassium channels and are useful for the treatment of "acute and chronic pain, migraine, neuropathic pain, bipolar disorders, convulsions, mania, epilepsy, anxiety, depression and neuro-degenerative disorders".

The Examiner compared the similarity of Applicants' R¹ substituent with the compounds of Grell, *et al.* Applicants wish to direct the Examiner's attention to the opposite side of the formula (see Formula I and Formula Ia in the Abstract and, more specifically, in Claim 1 of the cited reference) wherein Grell, *et al.* discloses compounds

having a phenyl ring substituted with a $\text{—N} \begin{array}{l} \text{R}_1 \\ \text{R}_2 \end{array}$ group. The instant compounds also have a phenyl ring, but are substituted with a Het substituent in the meta position of the phenyl ring.

In the Grell, *et al.* compounds, the substitution on the phenyl ring is directly through the nitrogen atom and, preferably, at the ortho position. On the other hand, Applicants phenyl ring is substituted with a heterocyclic group mainly through a carbon atom, except for the imidazole [Examples 7, 28, 32], pyrazole [Examples 4, 31] and triazole [Example 2] groups which are not disclosed in the cited reference. As a result, Applicants believe that there is no overlap of substitution pattern and heterocyclic groups in the phenyl ring on the opposite side of the formula for compounds as listed for R₁ and R₂ substituents in column 3, line 37 to column 4, line 12 in the cited reference.

Applicants respectfully submit that the reference must be viewed as a whole for what it teaches and believe that when evaluated as a whole, is insufficient to render

obvious the instantly claimed compounds. The reference does not provide the required elements to suggest the desirability of making the specific combination for the use that was made by the Applicants in the present application. See In re Kotzab, 217 F. 3d 1369, 55 USPQ2d at 1316 (Fed Cir 2000).

In view of the foregoing amendments and remarks, Applicants believe that the rejections have been traversed and favorable action on the amended claims is respectfully solicited.

Respectfully submitted,



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Enclosure: Petition for Time Extension